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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/425,742	10/22/1999	KARL THEODOR KRAEMER	02481.1641	9957

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EXAMINER

YU, GINA C

ART UNIT PAPER NUMBER

1617

DATE MAILED: 03/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/425,742

Applicant(s)

KRAEMER ET AL.

Examiner

Gina C. Yu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 18 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-23, 28, 29 and 39-44 is/are pending in the application.
- 4a) Of the above claim(s) 3, 9 and 41-44 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 4-8, 10-23, 28, 29, 39, and 40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

In view of the board decision mailed on March 18, 2005, PROSECUTION IS HEREBY REOPENED. New grounds of rejections are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below:

Pursuant to the recommendation of the board, in claim 1, the phrase "wherein said compound of formula 1 is released from the film formed by application of said composition to a skin surface" was given patentable weight. The issue of whether the liposomes of Dubios and film-former of Cretois would have released the compound instant formula 1 was considered, as recommended by the board. In view of further search and consideration, the final rejection of claims made under 35 U.S.C. § 103 (a) for obviousness over Cretois in view of Dubios is withdrawn. Amendment filed after appeal, submitted on December 15, 2003, has been entered. New rejections are made.

The prosecution history of this case indicates that applicants have elected polyvinylpyrrolidone/imidazolinium methochloride copolymers and ethoxylated hydrogenated castor oil as the representative film-forming agent and plasticizer of a formulation which represents the present invention. See Office action dated November 15, 2000. Newly added claim 39 40 read on this elected species, and claims 41-44 are withdrawn from consideration.

Claims 1-23 and 28, 29, 39-44 are pending, of which claims 3, 9, 41-44 are withdrawn from consideration.

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly et al. (US 5411981) in view of Partain, III et al. (US 4946870) and Encyclopedia of Controlled Drug Delivery, (Vol. 1 & 2, 1999).**

Gaillard-Kelly et al. teach that the compound of instant formula I has anti-androgenic activity and is used in pharmaceutical compositions including creams, pomades, and lotions. See col. 9, lines 29 – 36. The reference teaches that the compositions useful for treatment of acne and androgenic alopecia, among others. See col. 9, lines 43 – 55. The reference specifically teaches that the compositions are “useful in dermatology” and can be used antiacne components such as retinol or with a product stimulating the growth of hair such as Minoxidil (6-amino-4-4-piperidino-1,2-

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dihydro-1-hydroxy-2-iminopyridimidine) for the treatment of alopecia. See col. 9, lines 56 – 65. See instant claims 11, 13, and 23. Example 96 teaches 4-[3-(4-hydroxybutyl)-2,5-dioxo-1-imidazolidinyl]-2-(trifluoromethyl)benzonitrile. See instant claim 4. The reference also teaches adding to the composition 5 alpha-reductase inhibitor, meeting instant claims 16 and 17. See col. 9, lines 56 – 61.

Partain teaches a topical film-forming composition for delivering pharmaceutical actives with controlled release. The reference teaches that the composition is useful as a delivery system for single or combination of pharmaceutical active agents, including antiacne agents (retinoic acid and benzoyl peroxide) and anti-alopecia agents (Minoxidil). See col. 9, lines 15 –16; Examples 1, 15, and 18. See instant claims 22, 23, 28, and 29. The reference also teaches using pharmaceutical actives including diazoxide and nifedipine, diltiazem are taught in col. 8, lines 55 – 58. See instant claims 11 and 12. The reference teaches that chitosan derivatives are useful film formers and topically applied in the form of lotion, solution, cream, etc. See col. 3, lines 28 – 52. The polymer is said to readily form a film and “acts as a reservoir to continuously deliver the actives as well as protect the tissue from further injury or insult”, which negates the need of hair cover. The reference goes on to teach that the film gives uniform distribution of the active on the tissue and prevents the migration or loss of the active from the site of application, and helps to control the dosage at a constant level. The reference also teaches using solvents including ethanol and glycerine with the chitosan film-forming agent. See col. 9, line 58 –66; col. 10, lines 10-17; Example 14.

Glycerine is a well-known plasticizer in controlled release pharmaceutical art. See Encyclopedia of Controlled Drug Delivery, p. p. 307, Table 1; p. 309.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teaching of Gaillard-Kelly by formulating a film-forming composition as motivated by Partain III because (a) both references teach anti-alopecia compositions; and (b) Partain teaches that its film-forming system delivers active agents, including anti-alopecia agents, with constant, controlled rate, and protects the applied area of the skin. The skilled artisan would have had a reasonable expectation of successfully producing a topical composition which releases the anti-alopecia agents in controlled manner.

**Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly, Partain, and Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of applicants' disclosure.**

The combined references fail to teach angiotensin converting enzyme inhibitors.

Lai teaches conjugates of dithiocarbamates with pharmacologically active agents, wherein dithiocarbamates are said to reduce cutaneous irritation and alopecia. See col. 3, lines 49-51. Captopril, fosinopril, felopdipine, nicardipine, and nifedipine are taught as pharmaceutical agents. See col. 8, lines 51-54.

It would have been obvious to one of ordinary skill in the art at the time the present invention was made to have modified the teachings of the combined references by adding to the composition captopril as motivated by Lai because all the references

are directed to treating alopecia, and Lai teaches captopril are combined with other anti-alopecia agents. The skilled artisan would have had a reasonable expectation of successfully producing a composition that treats alopecia and hypertension.

**Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly, Partain, and Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 11-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of Ismail (US 5541220) .**

Gaillard, Partain, and Encyclopedia of Controlled Drug Delivery fail to teach methylxanthine compounds.

Ismail teach agents for the treatment protection of the skin. Exemplified is a capsule that can treat alopecia comprising pentoxifylin, vitamin E, and other ingredients.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add pentoxifylin to the composition of the composition of the combined references because Ismail and the references are directed to treating alopecia and Ismail teach pentoxifyline as increasing blood circulation. The skilled artisan would have been motivated to add pentoxifyline to the composition of the combined references because of the expectation of circulating the active agents of the composition through the body.

**Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly, Partain, and Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of WO 92/21317.**

The combined references fail to teach 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide.

WO'317 teaches compositions containing a pyridine-1-oxide for combating hair loss and inducing/stimulating hair growth. See abstract. Specifically disclosed is 2,4-diamino-6-butoxy-3-sulfoxypyridimidine hydroxide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition of the combined references because WO '317 and the references are all directed toward combating hair loss. The skilled artisan would have been motivated to add 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition of the combined references because of the expectation of further combating hair loss.

**Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly, Partain, and Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 7, 8, 10-13, 16, 17, 22, 23, 28, and 29 as above, and further in view of WO 91/19701.**

The combined references fail to teach 2,6-diamino-1,3,5-triazine compounds.

WO'317 teaches compositions containing a pyridine-1-oxide for combating hair loss and inducing/stimulating hair growth. See abstract. Specifically disclosed is 2,4-diamino-6-butoxy-3-sulfoxypyridimidine hydroxide.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition of the combined references because WO '317 and the references are all

directed toward combating hair loss. The skilled artisan would have been motivated to add 2,4-diamino-6-butoxy-3-sulfopyrimidine hydroxide to the composition of the combined references because of the expectation of successfully producing an enhanced composition for combating hair loss.

**Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly, Partain, and Encyclopedia of Controlled Drug Delivery as applied to claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 as above, and further in view of Cremophor RH 40 Technical Information (1997).**

The combined references fail to teach polyoxyethylene hydrogenated castor oil.

Cremophor RH 40 Technical Information (Cremophor) teaches that POE hydrogenated castor oil is skin compatible and solubilizes hydrophobic pharmaceuticals including vitamin A (retinoic acid). See Solubilization. The reference teaches that the product forms clear solutions in water and ethanol with fatty acids and fatty alcohols. See Solubility.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of the combined references by adding to the composition POE hydrogenated castor oil as motivated by Cremophor because (a) Gaillard, Partain, and Cremophor all teach using retinoic acid; and (b) Cremophor teaches that POE hydrogenated castor oil is a well known solubilizer in pharmaceutical/cosmetic art, which solubilizes hydrophobic pharmaceutical agents to form a clear solution. The skilled artisan would have had a reasonable expectation of

successfully producing a stable, clear cosmetic composition comprising retinoic acid and the compound of instant formula (I).

**Claims 1, 2, 4, 8, 10-13, 22, 23, 28, 29, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gaillard-Kelly in view of Smith (US 5658559) and Encyclopedia of Controlled Drug Delivery.**

Gaillard and Encyclopedia of Controlled Drug Delivery are discussed above.

Smith teaches a film-forming lotion composition which forms barrier on the surface of the skin to prevent evaporative loss of moisture from the skin, and protects the skin from environmental irritants. Polyvinylpyrrolidone/eicosene copolymers, polyvinylpyrrolidone/vinyl acetate copolymers, and polyvinylpyrrolidone/hexadecane copolymers are taught in col. 4, lines 14 – 32. See instant claim 10. The composition also contains polysaccharide polymers which release the therapeutic agents in a time-controlled manner. See col. 4, lines 33 – 43. Also taught is polyquaternary polyvinylpyrrolidone such as polyquaternium-16 (polyvinylpyrrolidone/imidazolinium methochloride copolymers). See instant claims 39 and 40. The therapeutic agents include antiacne actives. See col. 5, lines 1-6. The composition of the invention comprises water and polyhydric alcohols such as propylene glycol and glycerol (plasticizer and solvent). See col. 8, lines 1 – 38. See instant claim 7.

It would have been obvious to one of ordinary skill in the art at the time the present invention was made modify the teaching of Gaillard by formulating a topical composition comprising the compound of instant formula (I) in the occlusive, film-forming lotion as motivated Smith because (a) both references are directed to acne

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treatment compositions ; and (b) Smith teaches that the film-forming formulation provides controlled-release of the actives while protecting the skin and prevent loss of moisture of the skin. The skilled artisan would have had a reasonable expectation of successfully producing a stable and effective film-forming lotion which is useful for treating acne or alopecia.

### ***Conclusion***


No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gina C. Yu whose telephone number is 571-272-8605. The examiner can normally be reached on Monday through Friday, from 7:00AM until 4:30 PM..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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